REMARKS

Status of the Claims

Claims 1-36 are currently pending in this application. Claims 30, 31, 35 and 36 were withdrawn from consideration as being drawn to non-elected subject matter. Claims 1-29 and 32-34 were rejected. Claims 14-17, 30, 31, 35 and 36 have now been canceled, and claims 1 and 32 have been amended. Support for amended claims 1 and 32 may be found throughout the specification as filed, for example, at page 4, line 18 – page 5, line 4, in Example 1, and in original claim 16. Thus, no new matter has been introduced by way of these amendments. Upon entry of the amendments, claims 1-13, 18-29 and 32-34 will be pending. Entry of the amendments and reconsideration in view of the following comments is respectfully requested.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Election/Restriction and IDS

Applicants appreciate the Examiner's acknowledgement of Applicants' election of Group I without traverse and her consideration of materials in the Information Disclosure Statements (IDS) submitted on February 10, 2005 and July 29, 2005.

Rejections Under 35 U.S.C. § 102(b)

Anticipation by Lopez-Sabater

Claims 1, 4-7, 11-12, 14-18, 21-24 and 28-29 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Lopez-Sabater *et al.* (*Lett. Appl. Microbiol.* 1997, 24:101-104;

hereinafter "Lopez-Sabater"), which allegedly teaches a method for the magnetic immunoseparation for detection of viral sequences by PCR.

Applicants respectfully traverse this rejection for the reasons set forth below.

The legal standard for anticipation under 35 U.S.C. § 102 is one of strict identity. *Trintec Industries, Inc. v. Top-U.S.A. Corp.*, 63 U.S.P.Q.2d 1597 (Fed. Cir. 2002). To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention. *In re Paulson*, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994) (citing *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990)). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131.

As a preliminary matter, claim 1 has been amended to recite the following new limitation: "...a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity..., wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof." Claims 14-17 have been canceled, thereby rendering moot all comments directed to these claims.

Lopez-Sabater teaches using Streptavidin MagneSphere® Paramagnetic beads (Promega) coated with biotinylated human anti-HAV (Hepatitis A virus) IgG (page 102, emphasis added). Thus, the method of separation taught by Lopez-Sabater, much like many other prior art references, is based on the highly specific binding between antigen and antibody, which is one of the binding modes expressly excluded from claim 1 as amended. Lopez-Sabater does not contain any teaching, express or implied, for using a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity, wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a

lipid and a complex thereof, as required by the presently amended claim 1. Since Lopez-Sabater fails to teach each and every element of claim 1 and claims depending therefrom, the strict identity standard of anticipation under 35 U.S.C. § 102 is not satisfied. Accordingly, Applicants respectfully submit that this rejection under 35 U.S.C. § 102(b) may now be withdrawn.

Anticipation by Olsvik

Claims 1-4, 6-10, 12-15, 17-18, 22-23, 27-28 and 32-34 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Olsvik *et al.* (*Clin. Microbiol. Rev.* 1994, 7:43-54; hereinafter "Olsvik"), which allegedly provides an overview of immunomagnetic separation using paramagnetic particles coated with antibodies for isolation of eukaryotic cells.

Applicants respectfully traverse this rejection for the reasons set forth below.

The legal standard for anticipation has been described above and is incorporated herein. As discussed above, both claims 1 and 32 have been amended to recite the following new limitation: "...a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity..., wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof." Claims 14-17 have been canceled, thereby rendering moot all comments directed to these claims.

Olsvik provides a general overview of immunomagnetic separation techniques used in diagnostic microbiology, including immunomagnetic purification and concentration of bacteria and viruses and amplification of nucleic acids by PCR. In the very first paragraph, Olsvik teaches that "immunomagnetic separation (IMS), i.e., using small super-paramagnetic particles or beads coated with antibodies against surface antigens of cells, has been shown to be efficient for the isolation of certain eukaryotic cells from fluids such as blood..." (page 43, emphasis added). Thus, much like Lopez-Sabater, Olsvik does not contain any teaching, express or implied, for using a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity, wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a

peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof, as required by the presently amended claims 1 and 32. Since Olsvik fails to teach each and every element of claims 1 and 32 and claims depending therefrom, the standard of anticipation under 35 U.S.C. § 102 is not satisfied. Accordingly, Applicants respectfully submit that this rejection under 35 U.S.C. § 102(b) may now be withdrawn.

Rejections Under 35 U.S.C. § 103(a)

Obviousness over Lopez-Sabater in View of Miltenyi

Claim 19 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Lopez-Sabater as applied to claims 1, 4-7, 11-12, 14-18, 21-24 and 28-29 above and further in view of Miltenyi *et al.* (U.S. Pat. No. 5,691,208; hereinafter "Miltenyi"). Lopez-Sabater teaches a method for the magnetic immunoseparation for detection of viral sequences by PCR. The Examiner acknowledged that Lopez-Sabater does not teach that the method is automated. To cure that deficiency of Lopez-Sabater, the Examiner cited Miltenyi, which allegedly teaches magnetic separators and devices for magnetic separation of cells. The Examiner concluded that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the automated format of Miltenyi to the method of cell isolation and amplification to arrive at the claimed invention with a reasonable expectation for success.

Applicants respectfully traverse this rejection for the reasons set forth below.

The Examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). The obviousness analysis under 35 U.S.C. § 103(a) requires the consideration of the scope and content of the prior art, the level of skill in the relevant art, and the differences between the prior art and the claimed subject matter must be considered. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966)). To establish a *prima facie* case of obviousness a three-prong test must be met. First, the prior art must reference must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d

981, 985 (CCPA 1974). Second, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference to achieve the claimed invention. *KSR* at 1731. And third, there must be a reasonable expectation of success found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Rejections on obviousness grounds cannot be sustained by mere conclusory statements. *In re Kahn*, 441 F.3d 977, 987-88 (Fed. Cir. 2007) (citations omitted). Critical elements of the invention as a whole which clearly distinguish the entire invention from the prior art references cannot be ignored. *Panduit Corp. v. Dennison Manufacturing Co.*, 1 U.S.P.Q.2d 1593, 1597 (Fed. Cir.), *cert. denied*, 481 U.S. 1052 (1987). Evidence of an unobvious or unexpected advantageous property can rebut prima facie obviousness. MPEP § 716.02(a). Moreover, if a proposed modification changes the principle of operation of a reference, the teachings of that reference are not sufficient to render the claimed invention obvious. MPEP § 2143.01.VI, citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959) (emphasis added).

The teachings of Lopez-Sabater and the current amendments to claim 1, from which claim 19 depends, have been discussed in detail above. Miltenyi teaches improved magnetic separators, devices and automated methods for magnetic separation. Much like Lopez-Sabater, Miltenyi does not teach or even suggest using a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity, wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof, as required by the presently amended claim 1. Obviously, there is a fundamental difference between separations based on highly specific antigen-antibody interactions and separations based on non-specific interactions. Since the problems to be solved are radically different, a person of ordinary skill in the art would not have been motivated to modify the teachings of Lopez-Sabater to achieve the present invention. Moreover, since the present invention has a different principle of operation than the one disclosed in the cited references, the teachings of these references are clearly insufficient to render the present invention obvious under *In re Ratti*.

Thus, neither of the cited references, alone or in combination, teaches or suggests using a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity, wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention. Moreover, the present invention has altered the fundamental principle of operation of the cited references, effectively rebutting the obviousness argument. Therefore, Applicants respectfully submit that the Office has failed to make a *prima facie* case of obviousness and this rejection under 35 U.S.C. § 103(a) may be withdrawn.

Obviousness over Olsvik in View of Inuma

Claims 20 and 25-26 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Olsvik as applied to claims 1-4, 6-10, 12-15, 17-18, 22-23, 27-28 and 32-34 above and further in view of Inuma *et al.* (*Int. J. Cancer* 2000, 89:337-44; hereinafter "Inuma"). Olsvik provides an overview of immunomagnetic separation using paramagnetic particles coated with antibodies for isolation of eukaryotic cells. The Examiner acknowledged that Olsvik does not teach a specific time frame (claim 20) or sample volume (claim 25) for practice of the invention, or that the target cells may comprise leukocytes (claim 26). To cure these deficiencies of Olsvik, the Examiner cited Inuma, which allegedly teaches specific targeting of leukocytes by magnetic beads comprising antibodies. The Examiner concluded that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have applied the teachings of Inuma to the method of immunomagnetic separation taught by Olsvik to arrive at the claimed invention with a reasonable expectation for success.

Applicants respectfully traverse this rejection for the reasons set forth below.

The legal standard for obviousness, the teachings of Olsvik, and the current amendments to claim 1, from which claims 20, 25 and 26 depend, have been discussed in detail above. Inuma teaches highly specific separation of $CD45^+$ cells using magnetic microbeads coated with anti-CD45

antibodies (page 338, emphasis added). Much like Olsvik, Inuma does not teach or even suggest using a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity, wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof, as required by the presently amended claim 1. Obviously, there is a fundamental difference between separations based on highly specific antigen-antibody interactions and separations based on non-specific interactions. Since the problems to be solved are radically different, a person of ordinary skill in the art would not have been motivated to modify the teachings of Olsvik to achieve the present invention. Moreover, since the present invention has a different principle of operation than the one disclosed in the cited references, the teachings of these references are clearly insufficient to render the present invention obvious under *In re Ratti*.

Thus, neither of the cited references, alone or in combination, teaches or suggests using a magnetic microbead not comprising a biomolecule that binds to said target cell or virus with high specificity, wherein said biomolecule is selected from the group consisting of an antibody, an amino acid, a peptide, a protein, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a vitamin, a monosaccharide, an oligosaccharide, a carbohydrate, a lipid and a complex thereof. In the absence of a teaching or suggestion of each and every claim element, the cited combination fails to provide the motivation to practice the presently claimed invention. Moreover, the present invention has altered the fundamental principle of operation of the cited references, effectively rebutting the obviousness argument. Therefore, Applicants respectfully submit that the Office has failed to make a *prima facie* case of obviousness and this rejection under 35 U.S.C. § 103(a) may be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 514572000700. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: June 3, 2008

Respectfully submitted,

By: /Yan Leychkis/
Yan Leychkis
Registration No.: 60,440
MORRISON & FOERSTER LLP
12531 High Bluff Drive, Suite 100
San Diego, California 92130-2040
(858) 314-7702